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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/069,465	01/29/2003	John David Windass	SYN-125	3406

22847 7590 01/27/2006

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EXAMINER	
WONG, JENNIFER SHIN SHIN	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 01/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/069,465	WINDASS ET AL.	
	Examiner	Art Unit	
	Jennifer Wong	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-55* is/are pending in the application.

4a) Of the above claim(s) *14-22,25-33 and 51-55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13,23,24 and 34-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 April 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *April 8, 2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1-13, 23-24, and 34-50, methods to detect a mutation by assaying for a polymorphism, in the reply filed on November 14, 2005 is acknowledged.

Claims 14-22, 25-33, and 51-55 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-13, 23, 24, 34-50 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an amino acid change of a glycine to alanine at the 143 codon ($G_{143}A$) caused by a guanine to cytosine (G to C) mutation in the second basepair of said codon in a fungal nucleic acid in a *S.cerevisiae* cytochrome b gene that gives rise to azoxystrobin resistance, does not reasonably provide enablement for any mutation in a fungal nucleic acid that gives rise to any strobilurin analogue or other compound in the same cross resistance group in a mitochondrial

gene. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The following factors have been considered in formulating this rejection (*In re Wands,* 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988): the breadth of the claims, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, the amount of direction or guidance presented, the presence or absence of working examples of the invention and the quantity of experimentation necessary.

Breadth of the Claims

The claims are broadly drawn to methods to detect a mutation in a fungal nucleic acid that results in a fungal resistance to strobilurin analog or any other compound in the same cross resistance group by assaying for the presence of the mutation present in the fungal nucleic acid. The claims are further drawn towards hybridization methods involving polymerase chain reaction (PCR) wherein the method comprises contacting a test sample with a diagnostic primer and the detection of said amplified product wherein the mutation indicates resistance to strobilurin analogs or other compounds in the same cross resistance group.

Nature of the invention

The invention is in a class of inventions that the CAFC has characterized as "the unpredictable arts such as chemistry and biology" (Mycolgen Plant Sci., Inc. v Monsanto Co., 243 F.3d 1316, 1330 (Federal Circuit 2001)).

Teachings in the Specification

The specification teaches strobilurin and strobilurin analogs are fungicides that inhibit fungi by "blocking the ubiquinol:cytochrome c oxidoreductase complex (cytochrome bc1) thus reducing the generation of energy rich ATP in the fungal cell....This family of inhibitors prevents electron transfer at the ubiquinone redox site Qo on the multimeric cytochrome b protein" (page 2). Fungicides are of particular importance because agriculture industry utilizes drugs such as strobilurin and strobilurin analogs to control fungi pathogens. Research of the molecular mechanisms underlying fungal resistance indicates several natural mutations in the cytochrome b gene of that plays a role in strobilurin resistance wherein "amino acid changes at residues 126, 129, 132, 133, 137, 142, 143, 147, 148, 256, 275 and 295 have been shown to give rise to resistance to strobilurin analogues" (page 2). The specification teaches "we have found that the position in the fungal cytochrome b nucleic acid corresponding to the 143rd codon/amino acid in the cytochrome b of *S.cerevisiae* sequence is a key determinant of fungal resistance to strobilurin analogues or any other compound in the same cross resistance class" in fungi resistant to said drugs (page 6). The specification further teaches the presence of a substitution from guanine to cytosine nucleotide change in the second position of the 143 amino acid of said gene results in an amino acid change from glycine to alanine results in a strobilurin resistance (page 7). Single nucleotide polymorphism (SNP) detection methods well known in the art involving PCR amplification are disclosed as tools to detect said mutation wherein diagnostic primers of said mutation are hybridized with test samples and the presence of said mutation

indicates strobilurin resistance. The specification provides four working examples of detecting resistance to azoxystrobin, a strobilurin analog, by assaying for $G_{143}A$ mutation caused by a G to C substitution at the second position of said codon with Scorpion™ system from AstraZeneca Diagnostics. The examples disclose lab protocols to prepare samples and Scorpion™ method steps to detect and measure the frequency of the mutation.

State of the Art

Kraiczy et al (European Journal of Biochemistry, 1996) studied the basis of natural strobilurin resistance by the cloning of cytochrome bc1 complex and sequence comparison of resistant mutants to controls. Karczy teaches "we sequenced the cytochrome b genes of all three basdiomycetes (two species resistant to strobilurin, *Strobilurs tenacellus and Mycena galopodia*, and a control *Mycena virdimaginata*). Using this combined approach, we could correlate inhibitor resistance to strobilurin A...with specific deviations from the consensus amino acid sequence of two cytochrome b domains" (page 55). Kraiczy teaches five SNPs that lead to strobilurin resistance: $T_{127}I$, $G_{143}A$, $A_{153}S$, mutations at positions 254 by glutamate, and Asn_{261}Aspartate (page 54). Kraiczy further analyzed the respiration rates of said species with different fungicides, including two strobilurin analogs strobilurin A and myxothiaol, as well as other mutations present in the different species (Table 1, page 57, and Figure 5, page 61). Esposti et al (Biochimica et Biophysica Acta, 1993) performed a sequence comparison of "ten partial primary sequences of cytochrome b...and they are compared with the sequence data from over 800 species for a detailed analysis of the natural

variation in the protein....The comparison of inhibition titrations in combination with the analysis of the primary structures has enabled us to identify amino acid residues in cytochrome b that may be involved in binding of the inhibitors" (page 244). As stated earlier, strobilurin analogs and others in its cross resistance class affect the Qo site on in cytochrome b. Esposti teaches eighteen different mutations that also play a role in myxothiaol resistance, including $G_{143}A$ (Table IV, page 262). Brasseur et al (Biochimica et Biophysica Acta, 1996) further provides two tables that "is possibly exhaustive and includes all cyt b mutants of prokaryotic...and mitochondrial (S. cerevisiae and others eukaryotes) origin" (page 67), wherein said tables "summarized their salient properties with respect to the structure and function of cytochrome b and to the Q_o and Q_i sites" (page 61). Tables 1 lists single mutations in cytochrome b mutants), including $G_{143}A$ mutations, whereas Table 2 is a list of multiple mutations of non-functional cytochrome b mutants (Table 1, pages 63-65; and Table 2, pages 66-67. Bennoun et al (Genetics, 1991) teaches a $Phe_{129}Leu$ in mutant cytochrome genes. Bennoun cloned and sequenced said gene and teaches "the primary sequence of this cyt b gene provided the basis for a molecular and genetic analysis of mutation conferring resistance to [the strobilurin analog] myxothiaol" (page 335). Furthermore, Kim et al (Phytopathology, 2003) teaches a mutation $F_{129}L$ that was discovered by the cloning and sequence of the cytochrome b gene. Kim teaches "Prior to this study, field resistance in phytopathogenic fungi was exclusively associated with the cytochrome b gene (CYTB) mutations that result in a replacement of glycine by alanine at amino acid position 143 (G143A). More recently [in 2001], resistance...has been associated with a mutation

resulting in a F129L change (page 891). In short, multiple mutations present in strobilurin resistance as well as mutations at the mitochondrial cytochrome b gene Qo site where the mutations take place have been reported at the time of the invention and as recently as 2001.

The Relative Skill of Those in the Art

The level of skill in the art is deemed to be high.

The Predictability or Unpredictability of the Art and Degree of Experimentation

The art of predicting mutations that result in strobilurin resistance is highly unpredictable. As indicated by Kim's teachings, strobilurin resistant mutations are still being discovered. As a result, it is unpredictable mutations that correspond to strobilurin analogs and other compounds in the same resistance group in fungal mitochondrial genes without further unpredictable experimentation. While the skilled artisan could detect any number of mutations in fungal mitochondrial genes to determine if said mutations result in strobilurin resistance or compounds of the same cross resistance group, the outcome of such research cannot be predicted, and such further research and experimentation are both unpredictable and undue. The specification has taught that $G_{143}A$ mutations are present in *S.cerevisiae* cytochrome b genes lead to azoxystrobin resistance, however, it is silent about the remaining genes within the fungal genome present in mitochondrial genes such as those genes encoding proteins and enzymes involved in respiration and mitochondrial DNA as well as structures such as the inner and outer cell membranes, cristae, and matrix. Consequently, one skilled in the art would have to test all genes within the fungal

mitochondrial genome in order to determine which mutations in fungal nucleic acids result in strobilurin, or any analog in its resistance group. Moreover, there are numerous strobilurin analogs and other compounds within the same cross resistance group such as picoxystrobin, krexosim-methyl, trifloxystrobin, famoxadone, and fenamidone as cited in the specification (page 6, lines 14-16). Furthermore, members of the strobilurin analog cross resistance group include ß-methoxyacrylates, which also inhibit the cytochrome b complex of which strobilurin is a member, as well as the strobilurin analogs carboxin, flutolanil, triflumazid, dimefluazoxystrobinle, fluazinam, ICI A 5504, BAS 490F, and SSF126 as well as oudemanin A. (Leroux, Science, page 192). Due to the absence of information regarding other mutations outside of $G_{143}A$ present in *S.cerevisiae* cytochrome b genes resulting in fungal resistance to azoxystrobin, it is highly unpredictable if other fungal mitochondrial genes also give rise to resistance to other strobilurin fungicides, as each gene and strobilurin analogs and compounds in the same cross resistance group with the exception of azoxystrobin needs to be individually tested. As a result, the specification does not teach the person skilled in the art how to reasonably predict, without undue burden, the mutations correspond to fungal resistance to strobilurin or other compounds in the same cross resistance group present in *S.cerevisiae* mitochondrial genes.

Amount of Direction or Guidance Provided by the Specification

There are no teachings or quantitative data that indicate all possible combinations of mutations leading to resistance to strobilurin analogs and other compounds in the same cross resistance group in mitochondrial genes other than $G_{143}A$ mutations in

S.cerevisiae cytochrome b genes in fungal nucleic acids corresponding to azoxystrobin resistance. Furthermore, there are no teachings that such expression exists in other resistant mutants, or if such expression exists, which mutations result in which strobilurin analog or compound in the same cross resistance group in mitochondrial genes. Consequently, a person skilled in the art would have to individually test each gene in the fungal mitochondrial genome to in order to identify which mutation in the specific mitochondrial gene or genes that result in resistance to any strobilurin or member of the same cross resistance group. For example, the skilled artisan would have to individually test for mutations present in mitochondrial genes in fungi such genes encoding proteins and enzymes involved in respiration and mitochondrial DNA as well as structures such as the inner and outer cell membranes, cristae, and matrix that leads to resistance to strobilurin analogs or other compounds in the same cross resistance group such as picoxystrobin, krexosim-methyl, trifloxystrobin, famoxadone, fenamidone, ß-methoxyacrylates, carboxin, flutolanil, triflumazid, dimefluazoxystrobinle, fluazinam, ICI A 5504, BAS 490F, and SSF126 as well as oudemanin A. The specification does not teach the person skilled in the art how to reasonably predict, without undue burden, how to determine the mutations other than other than $G_{143}A$ mutations in *S.cerevisiae* cytochrome b genes in fungal nucleic acids corresponding to azoxystrobin resistance.

Working Example

The specification does not provide any working examples of methods to identify mutations in any mitochondrial gene with any SNP detection methods that result in strobilurin analog or other compounds in the same cross resistance group except for methods to detect $G_{143}A$ mutations caused by a G to C substitution in the second base of said codon in cytochrome b genes that leads to resistance to azoxystrobin. The specification does not provide working examples for the identification of any mutation resulting in mitochondrial resistance to any strobilurin analog or member of the same cross resistance group such as picoxystrobin, krexosim-methyl, trifloxystrobin, famoxadone, fenamidone, ß-methoxyacrylates, carboxin, flutolanil, triflumazid, dimefluazoxystrobinle, fluazinam, ICI A 5504, BAS 490F, and SSF126 as well as oudemanin A

Conclusions

Case law has established that '(t)o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" In re Wright 990 F.2d 1557, 1561. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) it was determined that '(t)he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art". The amount of guidance needed to enable the invention is related to the amount of knowledge in the art as well as the predictability in the art. Furthermore, the Court in Genentech Inc. v Novo Nordisk 42 USPQ2d 1001 held that '(I)t is the specification, not the knowledge of

one skilled in the art that must supply the novel aspects of the invention in order to constitute adequate enablement". In the instant case, the specification does not provide methods to enable the claimed method to detect the presence of the mutation responsible for strobilurin analog or compounds from the same cross resistance class because it does not establish which mutations are indicative of resistance to strobilurin analogs, or analogs of the resistance class and at which mitochondrial gene. In view of the high level of unpredictability in the art and lack of guidance provided by the specification and prior art, undue experimentation would be required to practice the claimed invention.

3. Claims 1-13, 23, 24, 34-50 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

In The Regents of the University of California B. Eli Lilly (43 USPQZd 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that 'An adequate written description of a DNA...'requires a precise definition, such as

by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention". In analyzing whether the written description requirement is met for a genus claim, it is first determined whether a representative number of species have been described by their complete structure. To determine whether a representative number of species have been described, one must first determine the scope of the claims. The most reasonable interpretation of the present claims indicates that claim $G_{143}A$ mutation in *S.cerevisiae* cytochrome b resulting in strobilurin resistance is inclusive of all mutations that result in resistance to strobilurin analogs or compounds in the same cross resistance group.

The claims are broadly drawn towards methods to detect a mutation in a fungal nucleic acid that results in a strobilurin analog or any other compound in the same cross resistance group by assaying for the presence of said polymorphism present in *S.cerevisiae* cytochrome b genes. The claims are further drawn towards hybridization methods involving polymerase chain reaction (PCR) wherein the method comprises contacting a test sample with a diagnostic primer and the detection of said amplified product wherein the mutation indicates resistance to strobilurin analogs or other compounds in the same cross resistance group.

In analyzing whether the written description requirement is met for a genus claim, it is first determined whether a representative number of species have been described by their complete structure. As indicated by research from Kraiczy, Esposti, Brasseur, Bennoun numerous mutations have been associated with strobilurin resistance in fungi known at the time of the invention, and Kim's recent teachings of a $F_{129}L$ mutation in

cytochrome b gene corresponding to strobilurin resistance indicate that other mutations are still being discovered. In the instant application, only the presence of one mutation, $G_{143}A$, in *S.cerevisiae* cytochrome b gene leading to resistance to azoxystrobin has been disclosed. Consequently, the combination of detecting the numerous mutations known in the art at the time of the invention as well as current and future mutations leading to resistance and its impact on strobilurin analogs and other compounds in its cross resistance class is immense. Each gene is characterized by its own unique and distinct chemical and structural compositions, and modulated by its interactions with other genes. As such, each gene's makeup, in turn, determines its function. The specification provides examples $G_{143}A$ mutation resulting in azoxystrobin resistance. However, the specification has not taught all mutations that give rise to resistance to all strobilurin analogs and members of the same cross resistance group in any mitochondrial gene. Consequently, a representative number of mutations in any mitochondrial gene resulting in strobilurin resistance has not been taught.

The limited information provided in the specification is not deemed sufficient to reasonably convey to one of skill in the art that Applicants were in possession of a representative number of mutations within the broadly claimed genus of mutations in a fungal nucleic acid wherein the presence of said mutation in a mitochondrial gene results in fungal resistance to strobilurin analogs or compounds in the same cross resistance group. Therefore, the written description requirement has not been satisfied for the claims as they are broadly written. Applicants attention is drawn to the Guidelines for the Examination of Patent applications under 35 U.S.C. 112, ¶ "Written

Description" requirement, Federal Register, vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Claim Rejections - 35 USC § 112

4 The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

A) Claims 1, 5-7, 10, 13, 23, 24, 34, 36- 39, 41,44, 47-50 are indefinite because the claims contain information in parentheses, i.e. "...any (or a) single nucleotide polymorphism technique...". Parentheticals make the claims indefinite because it is unclear whether the information in the parentheses has the same, less, or more weight as the rest of the claim language.

B) The term "around" in claims 23 and 24 is a relative term which renders the claim indefinite. The term "around" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably appraised of the scope of the invention. The term "around" makes the claim indefinite because it is unclear whether the information comprising up to 30 and more than 30 nucleotides includes sequences of the entire gene. Hence, it is what the sequence length is necessary to be used for the SNP detection method.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 5-8, 10, 11, 34, 35, 44, and 45 are rejected under 35 U.S.C. 102 (b) as being anticipated by Zheng et al (1997, as cited in the IDS).

Zheng teaches a method to detect strobilurin or strobilurin analog resistance in fungi by assaying for a single nucleotide polymorphism (SNP) wherein the method comprises the steps of 1) treating a crop with strobilurin and kresoxim-methyl, a strobilurin analog; 2) culturing and isolating fungi that are resistant to said drugs; 3) isolating total and mitochondrial DNA (tDNA and mDNA respectively); 4) PCR amplifying cytochrome b sequences; 5) detecting said amplified regions with Southern blots; as well as 6) cloning and sequencing said amplified mtDNA and comparing sequence results with controls. In particular, Zheng teaches strobilurins inhibit respiration by binding to mitochondrial cytochrome b genes, and "the cloning and characterization of the V. inaequalis cytochrome b gene is the initial step in the assessment of resistance risks inherent to the strobilurin fungicides" (page 361). Accordingly, Zheng teaches methods to detect strobilurin, or strobilurin analog,

resistance through PCR amplification and the detection of a mutation that results in fungicide resistance.

With respect to claims 1,2, 5-8, 34, 35, 37, 44, and 45, Zheng teaches methods to detect a mutation of a glycine to alanine at the 143 amino acid residue ($G_{143}A$) which results in a fungal resistance to the strobilurin or any strobilurin analog fungicides by sequencing the SNP site and comparing it to a control. Zheng's methods require treating an untreated crop with strobilurin and strobilurin analog, kresoxim-methyl. Zheng teaches "an experimental orchard at the New York State Agricultural Experiment Station in 1988...had never been treated with strobilurin fungicides, and...kresoxim-methyl" (page 362). Resistant fungal pathogens were subsequently cultured and tDNA and mDNA were isolated (page 362). Zheng teaches "based on four highly conserved regions of cytochrome b amino-acid sequences, the following degenerate PCR primers were designed, " including P3-F and P3-R primers:

"P3-F 5'-TTA(AG)GGTGC(AT)AC(AT)GT(TA)ATTAC-3'

and P3-R 5'-GTAAT(AT)AC(AT)GT(AT)GCACC(CT)CA-3'"

which is specific for "positions 142-148...of the S. cerevisiae cytochrome b" and "PCR amplifications with various primers were carried out" (page 364). Zheng teaches Southern hybridizations probed said primers are performed to determine appropriate size fragments to clone and sequence (page 362-363). Zheng further utilizes sequence analysis to compare amino acid changes between the resistant pathogen and controls, including $G_{143}A$ (table 1, page 364). Accordingly, Zheng teaches methods to detect

SNPs present in fungal nucleic acids wherein the presence of said mutation results in resistance to the fungicides strobilurin, and the strobilurin analog, kresoxim-methyl.

With respect to claim 10, the claim is broadly drawn toward fungal genes present in pathogenic fungi. Zheng applies said method to *Venturia inaequalis*, the pathogen responsible for apple scab (page 361).

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 3,4,9, 12, 13, 36-39, 46, 47, 49 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zheng in view of Landegren (Genome Research, 1998).

Zheng teaches a method to detect strobilurin or strobilurin analog resistance in fungi of *S.cerevisiae* cytochrome b gene by assaying for a single nucleotide polymorphism (SNP) wherein the method comprises the steps of 1) treating a crop with strobilurin and kresoxim-methyl, a strobilurin analog; 2) culturing and isolating fungi that are resistant to said drugs; 3) isolating total and mitochondrial DNA (tDNA and mDNA respectively); 4) PCR amplifying cytochrome b sequences; 5) detecting said amplified

regions with Southern blots; as well as 6) cloning and sequencing said amplified mtDNA and comparing sequence results with controls. In particular, Zheng teaches strobilurins inhibit respiration by binding to mitochondrial cytochrome b genes, and "the cytochrome b gene was cloned and sequenced from the mitochondrial genome of *Venturia inaequalis*, the causal agent of apple scab" (page 361). Through sequence analysis, Zheng identifies SNPs that are present in resistant fungal pathogens (page 364, Table 2). Accordingly, Zheng teaches methods to detect strobilurin, or strobilurin analog, resistance through PCR amplification and the detection of a mutation that results in fungicide resistance.

Zheng teaches methods to detect a mutation of a glycine to alanine at the 143 amino acid residue ($G_{143}A$) which results in a fungal resistance to the strobilurin or any strobilurin analog fungicides by sequencing the SNP site and comparing it to a control. Zheng's methods require treating an untreated crop with strobilurin and strobilurin analog, kresoxim-methyl. Zheng teaches "an experimental orchard at the New York State Agricultural Experiment Station in 1988...had never been treated with strobilurin fungicides, and...kresoxim-methyl" (page 362). Resistant fungal pathogens were subsequently cultured and tDNA and mDNA were isolated (page 362). Zheng teaches "based on four highly conserved regions of cytochrome b amino-acid sequences, the following degenerate PCR primers were designed, " including P3-F and P3-R primers:

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which is specific for "positions 142-148...of the S. cerevisiae cytochrome b" and "PCR amplifications with various primers were carried out" (page 364). Zheng teaches Southern hybridizations probed said primers are performed to determine appropriate size fragments to clone and sequence (page 362-363). Zheng further utilizes sequence analysis to compare amino acid changes between the resistant pathogen and controls, including $G_{143}A$ (table 1, page 364). Accordingly, Zheng teaches methods to detect SNPs present in fungal nucleic acids wherein the presence of said mutation results in resistance to the fungicides strobilurin, and the strobilurin analog, kresoxim-methyl.

However, Zheng does not teach the application of utilizing a method wherein the diagnostic primer is extended either when the mutation responsible for strobilurin resistance is present in the test or wild type samples, and the detection of said mutation wherein the presence indicates resistance to said drugs. Landegren teaches SNP detection methods comprising hybridization and amplification of test samples with labeled probes wherein mutant sequences are detected by the presence of primer extended products (1998).

Landegren teaches several detection methods of mutant sequences by assaying for primer extension wherein said extension indicates a SNP (entire document). Landegren teaches current methods "involve target sequence amplification, and this is followed by distinction of DNA sequence variants by short hybridization probes...discrimination of mismatched DNA substrates by polymerases or ligases; or by observing the template-dependant choice of nucleotide incorporation by a polymerase" (page 770). Landegren teaches TaqMan, molecular beacons,

oligonucleotide ligation, ligase chain reaction, minisequencing assays to detect sequence variants. Landegren teaches that TaqMan and molecular beacon assays detect SNPs utilizing PCR reactions. In TaqMan assays, a labeled diagnostic primer is designed for the sequence region of interest, and a TaqMan probe that has a labeled donor-acceptor dye is designed downstream immediately adjacent to the diagnostic probe. During PCR amplification, Taq polymerase digests the 5' end of the diagnostic primer, and thereby annealing the two probes and with the interaction of the two probes, the fluorophores is quenched resulting in increased fluorescence. Landegren further teaches said method is a "closed-tube, walk-away assay is relatively fast and it minimizes PCR contamination" and "fluorescence can be detected when an allele-specific oligonucleotide hybridizes to a target molecule" (page 771-772). Molecular beacons, on the other hand, have a complementary sequence adjacent to the target region and a donor-acceptor dye pair at the terminal ends of the primer. When the probe does not bind to the target, it adopts a hairpin loop structure and thereby inhibiting fluorescence. However, when the probe binds to the target region, the two dyes are separated and "fluorescence increases by up to 900-fold" (page 771). Landegren also teaches that the allele sensitivity is increased with molecular beacons because of low stringency PCR conditions during PCR annealing steps and different dye spectra allowing multiple molecular beacons used in assays as each beacon can be labeled differentially (page 771). Landegren also teaches that ligation assays can be used to detect SNPs (pages 771-772). In this method, there are two probes that abut the SNP, and during ligation, if there is hybridization with the target sequence,

DNA ligases join the two probes and the joined probes can be detected as they can be labeled with dyes and the procedure can be performed on an array thus allowing for high throughput analysis. Oligonucleotide ligation and ligase chain reaction assays differ from one another in that in the former the sequence flanking the SNP is PCR first PCR amplified whereas the latter method, genomic DNA can be used as template. Landegren further teaches DNA ligation assays requires high stringency conditions for "correct base pairing on the 3' end of the hybridizing primers. This can be used to selectively amplify one or the other allele of an SNP....This method also offers a unique advantage in that it permits analysis of the linkage phase of two neighboring SNPs, provided these are located sufficiently close, by use of allele-specific PCR primers at both ends of the amplification product" (page 772). Landegren further teaches that said method is "quite sensitive to mismatches close to the ligation site" wherein difficult mismatches can be detected (page 772). Hybridization of the diagnostic primer and sequence variance can be detected when the allele-specific probes are fluorescently labeled, and "analyzed via time-resolved fluorometry...[and] dual-color detection of allele-specific ligation products is also possible in a regular spectrophotometer" (pages 772-773). Minisequencing, on the other hand, involves "target-dependent addition [of a nucleotide] by a DNA polymerase of a specific nucleotide to a single primer" wherein complementary binding to a target region is detected by measuring fluorescence when the correct incorporated nucleotide hybridizes to the target region (page 773). Landegren further teaches that minisequencing "distinguishes more accurately between variable nucleotides located immediately downstream of the primer than is possible by

use of the differential stability of hybridization by allele-specific probes" (page 773). Moreover, Landegren also teaches the advantages of said DNA amplification techniques "highly specific detection of unique DNA sequences...by requiring two target recognition events, one by each primer, to detect a particular sequence" however, in order to prevent false priming during PCR reactions, "longer hybridization probes may [aid] identify[ing] a unique sequence," however, one disadvantage is that longer probes are less specific for SNPs. (pages 773-774). Moreover, SNP detection occurs when "extension of a dye-labeled nucleotides is observed via fluorescence detection" (page 773). Accordingly, Landegren teaches SNP detection methods by primer extension during PCR amplification, the identification of SNPs by the hybridization of a diagnostic primer and target sequence, and quantifying the presence of said SNPs by the amount of fluorescence.

It would have been prima facie obvious at the time the invention was made to modify the teachings of Zheng with the improvement of Landegren because Zheng teaches methods to detect the presence of the $G_{143}A$ mutation wherein said mutation corresponds to strobilurin and strobilurin analog resistance by a sequencing SNPs, and Landegren teaches SNP detection methods by primer extension during PCR amplification and quantifying SNPs by the amount of fluorescence of labeled allele-specific probes. A person skilled in the art at the time of the invention would have been motivated to have used PCR amplification methods involving primer extension in order to achieve the benefit of increased sensitivity to detect SNPs, ease in performing less time consuming assays and measuring the presence or absence of SNPs, as well has

high throughput analysis. The skilled artisan would have been motivated to design primers with G to C mutation in the second position of the $G_{143}A$ because Zheng teaches that said mutation results in strobilurin resistance. Without knowing the exact nucleotide SNP of the $G_{143}A$ mutation that results in fungicide resistance, one would inherently design primers to distinguish all possible nucleotide combinations that would result in the $G_{143}A$ mutation. Designing primers which are equivalents to those taught in the art is routine experimentation. The parameters and objectives involved in the selection of primers were well known in the art at the time the invention was made and software programs were readily available which aid in the identification of conserved and variable sequences and in the selection of optimum primer pairs. The ordinary artisan would have had more than a reasonable expectation of success of using primers with G to C mutation in the second position of the $G_{143}A$ with Landegren's methods to have sensitive, high throughput assays to detect strobilurin resistance. Thus for the reasons presented above, it would have been obvious to use Landegren's primer extension assays to detect SNP of $G_{143}A$ that is responsible for strobilurin resistance.

8. Claims 23, 24, and 48 are rejected under 35 U.S.C. 103(a) as being obvious over Zheng in view of Whitcombe et al (U.S. Patent No. 6,326,145).

The applied reference has a common inventors with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome

by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Zheng teaches a method to detect a $G_{143}A$ mutation of *S.cerevisiae* cytochrome b gene, wherein the method comprises: 1) treating a crop with strobilurin and kresoxim-methyl, a strobilurin analog; 2) culturing and isolating fungi that are resistant to said drugs; 3) isolating total and mitochondrial DNA (tDNA and mDNA respectively); 4) PCR amplifying cytochrome b sequences; 5) detecting said amplified regions with Southern blots; as well as 6) cloning and sequencing said amplified mtDNA and comparing sequence results with controls as presented above. However, Zheng does not teach SNP detection methods involving Scorpion™ detection systems.

Whitcombe teaches SNP detection methods involving Scorpion™ detection systems wherein said method comprises: 1) obtaining a genomic sample from an organism; 2) hybridizing said sample with a diagnostic primer designed for sequence

variations with a hairpin loop configuration wherein the hairpin loop is joined by complementary sequences at the stem, a probe sequence for the sequence variant at the hairpin loop, a fluorophore and quencher, or PCR blocker, are at the respective the 5' and 3' ends of the base stem; 3) detecting fluorescence which is an indicator of hybridization of the diagnostic primer with the target region. Scorpion™ primers have a three dimensional hairpin structure wherein the self target regions hybridize to one anther, wherein the fluorophore and blocker are adjacent to one another with the fluorophore and blocker are at the 5' and 3' end of one another, and the diagnostic sequence is at the 3' end of the primer (Figure 2). During PCR amplification, the primer hybridizes to the target and extension occurs due to the action of polymerase, and the primer undergoes a conformation change wherein the hairpin loop opens and the probe region within the loop binds to the sequence variation thus releasing the fluorophore from the quencher and resulting in fluorescence. The blocker prevents false priming which may occur in the absence of the specific target sequence (Figure 10A-C). Whitcombe teaches that Scorpion™ primers can be used as a diagnostic tool to discriminate between SNPs and control sequences wherein there are several methods to detect SNPs: 1) there are standard primers and "different probe sequences to match...allelic variants...are introduced...on the same primer"; 2) probes for each variant are designed on different strands; 3) "different primers ...used...for allele discrimination and as control primers for amplicon detection" (column 12, lines 1-17; and column 12, lines 8-16; Figures 12a-e). Whitcombe teaches nucleic acids from fungi can be used as samples for analysis (column 6, lines 5-7). The advantages of

Scorpion™ primers include the ease of a "single primer/detector," signal detection based upon the amount of primer extended products which is "not dependant on additional hybridization events or enzymatic steps", the reduction of competition for the probe site" (column 2, lines 2-27). Further, Whitcombe teaches "we have found that probes which fail to bind under standard assay conditions in separate probe format work well under our invention" and that "as the interaction is unimolecular, the signaling reaction is very rapid, permitting increased cycle rates as well as clear signal detection as "backgrounds are low and signals are high allowing a good deal of flexibility in assay design" (column 2, lines 29-34; and column 8, lines 26-28).

It would have been prima facie obvious at the time the invention was made to modify the teachings of Zheng with the improvement of Whitcombe because Zheng teaches $G_{143}A$ mutation in *S.cerevisiae* cytochrome b gene that may give rise to strobilurin fungicide resistance and Whitcombe teaches Scorpion™ detection methods that allow for high sensitivity SNP analysis. A person skilled in the art at the time of the invention would have been motivated to have used Whitcombe's method in order to achieve the benefit of detecting $G_{143}A$ mutation in *S.cerevisiae* cytochrome b gene with the ease of using only one primer/detector in a reaction instead of several reagents in detecting for mutations the added benefit of a rapid assay with clear signal detection unimpeded by false priming or ambiguous signals due to errors in amplification from additional rounds of hybridization or enzymatic steps using the Scorpion™ detection methods. Moreover, the skilled artisan would have been motivated to have modified the teachings of Zhang so as to include the methods of Whitcombe because

Whitcombe teaches Scorpion™ methods have been able to detect expression that have failed under other laboratory protocols. Designing primers which are equivalents to those taught in the art is routine experimentation. The parameters and objectives involved in the selection of primers were well known in the art at the time the invention was made and a person skilled in the art at the time of the invention would have been motivated to use Scorpion™ detection methods based on surrounding sequence of 30-90 basepairs upstream and/or downstream of $G_{143}A$ mutation of *S.cerevisiae* cytochrome b in order to have achieved the benefit of unimolecular interaction efficiency. Whitcombe teaches "the spacing on a DNA strand between the amplicon binding region and its complementary sequence within the amplicon may be as little as 30 bp (that is directly abutting the primer region) or may be as much as about 200-300 bases. The efficiency of the unimolecular interaction is expected to decline as this distance increases" (column 7, lines 60-64). Software programs were readily available at the time the invention was made which aid in the identification of conserved and variable sequences and in the selection of optimum primer pairs. The skilled artisan would have been motivated to design primers with G to C mutation in the second position of the $G_{143}A$ because Zheng teaches that said mutation results in strobilurin resistance. Without knowing the exact nucleotide SNP of the $G_{143}A$ mutation that results in fungicide resistance, one would inherently design primers to distinguish all possible nucleotide combinations that would result in the $G_{143}A$ mutation. The skilled artisan would have been motivated to design primers 30-90 bp upstream and/or downstream of the $G_{143}A$ mutation with the G to C substitution in said codon because a

primer design that is further away from the sequence of interest loses the Scorpion™ advantages of high sensitivity, clear signal detection, and time efficacy that is due to unimolecular interactions. As a result, if the skilled artisan will have a highly sensitive method to detect $G_{143}A$ mutations as well as improved time efficiency and cost savings by performing this assay that requires fewer reagents due to one primer/detector. Further, the ordinary artisan would have had more than a reasonable expectation of success of obtaining primers based upon sequences 30-90 upstream and/or downstream of $G_{143}A$ mutation of *S.cerevisiae* cytochrome b gene. Thus, for the reasons provided above, the use of primers of 30-90 upstream and/or downstream of $G_{143}A$ mutation of *S.cerevisiae* cytochrome b gene with a G to C mutation in the second position of said codon of would have been obvious to one of ordinary skill in the art.

9. Claims 40-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zheng in view of Whitcombe in further view of Corran et al (Pesticide Science, 1998).

The applied reference has a common inventors with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR

1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Zheng teaches a method to detect a $G_{143}A$ mutation of *Venturia inaequalis*, wherein the method comprises: 1) treating a crop with strobilurin and kresoxim-methyl, a strobilurin analog; 2) culturing and isolating fungi that are resistant to said drugs; 3) isolating total and mitochondrial DNA (tDNA and mDNA respectively); 4) PCR amplifying cytochrome b sequences; 5) detecting said amplified regions with Southern blots; as well as 6) cloning and sequencing said amplified mtDNA and comparing sequence results with controls as presented above. However, Zheng does not teach methods to select a fungicide and application of optimal application levels to a crop by Scorpion™ methods to detect the presence of a $G_{143}A$ mutation in that may give rise to strobilurin fungicide resistance.

Whitcombe teaches SNP detection methods involving Scorpion™ detection systems wherein said method comprises: 1) obtaining a genomic sample from an organism; 2) hybridizing said sample with a diagnostic primer designed for sequence variations with a hairpin loop configuration wherein the hairpin loop is joined by complementary sequences at the stem, a probe sequence for the sequence variant at the hairpin loop, a fluorophore and quencher, or PCR blocker, are at the respective the

5' and 3' ends of the base stem; 3) detecting fluorescence which is an indicator of hybridization of the diagnostic primer with the target region. The advantages of Scorpion™ primers include the ease of a "single primer/detector," signal detection based upon the amount of primer extended products which is "not dependant on additional hybridization events or enzymatic steps", the reduction of competition for the probe site" (column 2, lines 2-27). Further, Whitcombe teaches "we have found that probes which fail to bind under standard assay conditions in separate probe format work well under our invention" and that "as the interaction is unimolecular, the signaling reaction is very rapid, permitting increased cycle rates as well as clear signal detection as "backgrounds are low and signals are high allowing a good deal of flexibility in assay design" (column 2, lines 29-34; and column 8, lines 26-28).

Corran teaches methods of selecting a fungicide based upon the presence of a mutation, and its application to crops based upon the advent of genomic research in vitro methods that are used to study mechanism of fungal resistance and selection of fungicides. Corran teaches "high-throughput in-vitro screens...aid the discovery of fungicides with novel modes of action....genetic information is beginning to have a major impact both on the way in-vitro targets are selected and on the speed at which mode-of-action information is gained on current fungicides having an, as yet, undefined mode of action" (page 338). Using yeast as a model for fungi as they are sensitive to a majority of fungicides, Corran teaches growth inhibition of resistant using yeast mutants to varying concentrations of strobilurin analogs azoxystrobin and myxothiazol (Table 3, page 342). After the application of fungicides to yeast, resistant clones were

subsequently sequenced and sequence analysis was performed to compare resistant yeast sequences to a control and teaches several mutations are present in resistant yeast (Table 3, pages 342-343). One method step in sequencing involves the amplification of samples. In particular, Corran teaches the selection fungicidal levels wherein the least amount of fungicide correlates to viable levels of colonies wherein "inhibitors must first kill the wild-type yeast and we prefer inhibitors which are active at <20 $\mu g\ ml^{-1}$ in our tests...clones which were resistant to concentrations of inhibitor approximately four-fold greater than the concentration required to completely control the growth of the wild-type strain" (page 342). Corran further teaches "as we know more about the genetic make-up of pathogens and the differences between them and the host crops we hope that these new approaches will enable us to design safer pesticides that have less impact on the environment and have a good resistance profile" (page 343). Accordingly, Corran teaches methods to analyze varying doses of different strobilurin analogs to a resistant fungal model and desirable levels of optimal does of fungicides to crops.

It would have been prima facie obvious at the time the invention was made to modify the teachings of Zheng with the improvement of Whitcombe and Corran. Zheng teaches methods to detect the presence of the $G_{143}A$ mutation wherein said mutation corresponds to strobilurin and strobilurin analog resistance by a sequencing SNPs; Whitcombe teaches Scorpion™ methods to detect SNPs; and Corran teaches methods to screen varying concentration of doses strobilurin analogs with resistant fungi models by sequence analysis utilizing PCR amplification. A person skilled in the

art at the time of the invention would have been motivated to have used the fungicide dose screening method of Corran with Whitcombe's Scorpion™ SNP detection methods to detect Zheng's $G_{143}A$ mutation of *S.cerevisiae* cytochrome b gene that leads to strobilurin resistance order to have achieved the benefit of selecting a fungicide and determining an optimal dose of said fungicide to crops based upon the presence of $G_{143}A$ mutations in *S.cerevisiae* cytochrome b genes that result in strobilurin resistance. The skilled artisan would have been motivated to modify Zheng's method to employ Scorpion™ detection systems of Whitcombe because Whitcombe's method has the ease of using only one primer/detector in a reaction instead of several reagents in detecting for mutations the added benefit of a rapid assay with clear signal detection unimpeded by false priming or ambiguous signals due to errors in amplification from additional rounds of hybridization or enzymatic steps using the Scorpion™ detection methods. Moreover, the skilled artisan would have been motivated to have modified the teachings of Zhang so as to include the methods of Whitcombe because Whitcombe teaches Scorpion™ methods have been able to detect expression that have failed under other laboratory protocols. As a result, the skilled artisan has a rapid, highly sensitive, cost effective method to detect $G_{143}A$ mutation of *S.cerevisiae* cytochrome b gene that leads to strobilurin resistance. One skilled in the art at the time the invention was made would have been motivated to modify the methods of Zheng and Whitcombe with the improvement of Corran. Corran teaches determining the least amount of fungicide that has optimal antifungal properties to apply to crops based upon mutations based upon PCR amplification and sequencing. One skilled in the art would have been

motivated to identify the optimal fungicide dose in order to have achieved the benefit of financial savings by the application of the least amount of fungicide that provides the maximum antifungal properties. Since Scorpion™ detection methods also involve PCR amplification; it would have been obvious at the time that the invention was made to modify Corran's method so as to include Whitcombe's Scorpion™ detection methods in order to achieve the benefit of increased sensitivity to detect levels of fungicide. Moreover, with Scorpion™ detection methods able to detect both $G_{143}A$ mutations in *S.cerevisiae* cytochrome b genes that result in strobilurin resistance and doses of fungicide, the skilled artisan can pick the appropriate fungicide and its dose to a crop that is infected with fungus. Since Zheng teaches the $G_{143}A$ mutations in *S.cerevisiae* cytochrome b genes that result in strobilurin resistance, the skilled artisan using Scorpion™ detection methods to detect said mutation would know to apply non-strobilurin fungicides to infected crops that have said mutation. Similarly, if the skilled artisan using Scorpion™ detection methods to detect the $G_{143}A$ mutations and did not find said mutation in infected crops could then apply Corran's methods to determine the appropriate levels of fungicide. One skilled in the art at the time of the invention would have been motivated to modify Zheng's methods in view of Whitcombe in further view of Corran in order to achieve the benefit of choosing an optimal dose of fungicides that has least amount detrimental environmental effects by utilizing fungicides that are the most effective.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Wong whose telephone number is (571) 272-1120. The examiner can normally be reached on Monday-Friday; 8 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (571) 272-0745. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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1/19/06